

September 4, 1979

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Dear Ken:

The additional reprints have been sent off and I hope that you receive them before too long. I was very sorry to miss Dr. Shiba's visit, but Theresa and Tom did give me both his and your regards.

There is very interesting news from the lab that you will want to know. Over the past six or eight months, in a variety of ways, we have made new and independent isolations of SV40 defectives. In essentially every isolation, one of the major new defective forms is very similar to, if not identical to, the defective whose sequence you determined. These defectives are especially prevalent when one passages wild type virus at 33 degrees, an observation that is consistent with recent experiments showing that your defective is replicated much more efficiently, at 33 degrees than at 37 degrees, compared to wild type SV40 DNA. In order to facilitate purification of the new defectives we have been incorporating them by recombinant DNA techniques into *E. coli*. Then we have plenty of material for analysis, free of any contaminating monkey sequences. Both by hybridization and by restriction analysis the similarity to your defective was already clear. Joseph Papamatheakis, a Fellow this year, has now sequenced one of these in part. It is essentially identical to your sequence in every place we have determined. This includes the joint between SV40 and monkey sequences to the right of the M-1 sequence, and, most surprisingly, the inversion and deletion in the SV40 sequence itself. We are writing some of this up and as soon as the preprints are ready I will send copies to you.

Needless to say we are very excited by all this since it suggests some measure of specificity in the viral-host interactions that give rise to these molecules. Tom McCutchan has prepared very pure probes of the unique monkey sequences by cloning parts of your defective in *E. coli*. He has used these to look for the sequences in genomic monkey DNA (after blotting restriction enzyme digests from gels to nitrocellulose). He found several bands, which fits with my old Cot curve data that suggested 13 copies of the sequence around the Bam site, within the monkey genome. He is currently

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involved in cloning these sequences from monkey in E. coli, and will then look at them to see just how similar they are to the sequence in the defective. We also have a hunch that the 33 base pair inverted SV40 sequence may in fact derive from the monkey genome itself.

You see then that the work you did and the sequence you determined has become the central point for a great deal more work, so you are always in our minds and conversations.

My family is very well indeed and I thank you for inquiring. We spent about ten days this summer at our house in the Caribbean and there we enjoyed the owl that your wife made. It looks wonderful on the wall there. I hope that you and your family are all very well too.

With best regards from everyone here,

Sincerely,

Maxine Singer